

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/007538

International filing date (day/month/year)
08.07.2004

Priority date (day/month/year)
08.07.2003

International Patent Classification (IPC) or both national classification and IPC
C07J1/00

Applicant
GLYCOMED SCIENCES LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
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Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

☒ paid additional fees.

☐ paid additional fees under protest.

☐ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

☐ complied with

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

☒ all parts.

☐ the parts relating to claims Nos.

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-27
	No: Claims	---
Inventive step (IS)	Yes: Claims	---
	No: Claims	1-27
Industrial applicability (IA)	Yes: Claims	1-27
	No: Claims	---

2. Citations and explanations

see separate sheet

Re Item IV

Lack of unity of invention

~~This Authority considers that there are 2 inventions covered by the claims indicated as follows:~~

- I: Claim 1-22,24-27 : A process for the preparation of steroid derivatives bearing in position 3 a triose moiety as claimed in claim 1.
- II: Claim 24 : Two new compounds namely tomatidin-3-yl triose and demissidin-3-yl triose.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The subject-matter of claims 1-22,24-27 concerns a process for the preparation of (potentially) known compounds whereas the subject-matter of claim 23 concerns new compounds. Thus, the prior art must be considered under two different aspects as there are two different technical problems to be solved, hence resulting in a non-unity.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: LI C ET AL: "Synthesis of diosgenyl alpha-l-rhamnopyranosyl-(1->2)-[beta-d-glucopyranosyl-(1->3)]-beta-d-glucopyranoside (gracillin)" CARBOHYDRATE RESEARCH, ELSEVIER SCIENTIFIC PUBLISHING COMPANY. AMSTERDAM, NL, vol. 306, no. 1-2, January 1998 (1998-01), pages 189-195, XP004204799 ISSN: 0008-6215 (GLYCOMED SCIENCES LTD ; SHAHID MOHAMMED (GB)) 6 March 2003 (2003-03-06)
- D2: ZOU C-C ET AL: "The synthesis of gracillin and dioscin: two typical representatives of spirostanol glycosides" CARBOHYDRATE RESEARCH, ELSEVIER SCIENTIFIC PUBLISHING COMPANY. AMSTERDAM, NL, vol. 338,

no. 8, 4 April 2003 (2003-04-04), pages 721-727, XP004417407 ISSN: 0008-6215

D3: IKEDA T ET AL: "Synthesis of neosaponins having an alpha-l-rhamnopyranosyl-(1->4)-[alpha-l-rhamnopyranosyl-(1->2)]-d-glucopyranosyl glyco-linkage" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 42, no. 12, 18 March 2001 (2001-03-18), pages 2353-2356, XP004229921 ISSN: 0040-4039

D4: WO 03/018604 A

D5: WO 2005/005454 A (GLYCOMED SCIENCES LIMITED; LAWSON, CHRISTOPHER, JOHN; WEYMOUTH-WILSON,) 20 January 2005 (2005-01-20)

D6: WO 2004/096830 A (GLYCOMED SCIENCES LIMITED; SHAHID, MOHAMMED) 11 November 2004 (2004-11-11)

D5 and D6 which are "E" documents not prior art according to the Chap II PCT proceedings.

Nevertheless, the extensive examination of that document, on the question whether it constitutes prior art or not, will depend essentially on the analysis of the claimed priority rights of the present application and will only be performed in the regional European proceedings to come.

Novelty of Invention 1 :

The subject-matter of the present application concerns the preparation of steroids bearing in position 3 a trisaccharidic moiety (saponins).

Since none of the available prior art discloses the claimed process, the subject-matter of invention 1 is considered new.

Inventive step of invention 1 :

D1, which is considered to represent the closest prior art, concerns the synthesis of saponins, consisting in synthesising the 1-->2 bond, then grafting the steroid and finally

synthetising the 1-->3 bond.

The subject-matter of present invention 1 mainly differs in that the 1-->2 bond is created, then steroid is grafted (and finally the 1-->2 bond is synthetised : see claim 12).

~~The problem to be solved can be regarded as providing an alternative process for the preparation of triose steroids.~~

in D1-D3, the coupling between the sugar part and the steroid is performed by reacting a steroid, an halo-glycoside and AgOTf, while in D4 an -S-Et glycoside may be used in combination with AgOTf. in every case a "similar" intermediate as the one depicted under Formula XIII (triflate intermediate) is obtained.

Thus, the subject-matter of claim 1 of invention 1 is merely considered as an adaptation of the prior art using a 1-->3 disaccharide (of formula XIII) instead of a 1-->2 disaccharide.

The claims 2-22 do not seem to contain particular features that a man skilled in the art could not perform either by knowing the cited prior art or with his general knowledge (in particular of protecting groups).

Thus, at present, the subject-matter of invention 1 is not considered inventive.

Novelty of Invention 2 :

The subject-matter invention 2 concerns tomatidin-3-yl and demissidin-3-yl derivatives bearing in position 3 a trisaccharidic moiety .

Since none of the available prior art discloses the claimed compounds, the subject-matter of invention 2 is considered new.

Inventive step of invention 2 :

As no use or activity or comparative tests, etc, are provided in the present application for the two claimed compounds of invention 2, is it not possible to formulate a problem to be solved by the compounds of invention 2.

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AUTHORITY (SEPARATE SHEET)**

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As new compounds are not patentable *per se*, no inventive step can be acknowledged for inventive 2.

Re Item VII

Certain defects in the international application

Claim 2 is dependant on itself instead of being dependant on claim 1 (Art. 6 PCT).